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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,353	04/27/2001	Gary Ruvkun	00786/351005	3561

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,353	RUVKUN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,13,17 and 19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1,13,21 and 22* is/are allowed.

6)☒ Claim(s) *17,19,20,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 01/25/06 has been acknowledged.

Claims 1, 13, 17, 19-24 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 17 and 19-20 and 23-24 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 07/22/05.

The instant claims are drawn to a method for screening candidate modulatory compounds for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity comprising: providing a C. elegans or isolated C. elegans cell expressing a gene that encodes any variant of SEO ID NO:54, SEQ ID NO:57, SEQ ID NO:102, human FKHR polypeptide or human AFX polypepide that functions in insulin signaling; and contacting the C. elegans or isolated C. elegans cell with a candidate

compound, wherein a decrease in expression or activity of the gene with the candidate compound identifies a candidate modulatory compound for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity.

At best the specification discloses the amino acid sequences of SEQ ID NO:54 which represent an amino acid motif at location 242-344 of *C. elegans* daf-16 protein (spec. page 77, para.2). Based upon the degree of amino acid homology (Spec. fig-21A), the specification teaches that FKHR and AFX are human orthologs of *C. elegans's* daf-16 (Spec. fig-21B). Besides the amino acid sequences of SEQ ID NO:54 **(def-16 motif)** the specification as filed fails to disclose what encompass a nucleic acid comprising any variant of SEQ ID NO:54 that functions in any insulin signaling pathway. Similarly the specification as filed fails to disclose any nucleic acid comprising any variant of SEQ ID NO:57 and 102 that hybridizes under stringent conditions to the nucleic acid encoding the amino acid sequences of SEQ ID NO:57 and 102 respectively and is capable of performing the asserted biological activity. *Furthermore, besides human FKHR and AFX encoding sequences the specification fails to disclose any other nucleic acid sequence that is a variant of SEQ ID NO:57 and SEQ:102, wherein the gene is obtained form any other organism and is capable of functioning like an insulin signals and convergence with DAF-7-like Smad signals. The specification as filed fails to identify the relevant characteristics of the nucleic acid sequences (as claimed) such that a person skilled in the art would recognize the other human FKHR and human AFX related nucleic acid sequences.*

Response to arguments

The applicant arguments regarding written description issue on pages 7-14 of response filed on 01/25/06 has been fully considered.

Regardng claims 1, 21 and 22 the applicant arguments has been found persuasive as claims has been amended to recite a human AFX or human FKHR polypeptides (rather than human AFX or human FKHR genes(s)). Regarding claim 1 (95% identity) the applicants arguments has been found persusive in view of fact that daf-16 is 71% identical to daf-16 and Dr. Gary Ruvkuns decllaration that demonstrated that FKHR can fucntionally substitute dor daf-16 in vivo.

Regarding 17 (hybridization variant) the applicant argues that the specification provides a written description of instant claims to satisfy the standard set forth by the Patent Office is its Written Description Guidelines and by the Federal Circuit in Lilly. The applicant argues that that office has provided no evidence that the variants as claimed would not have the claimed functional activity. The applicant argues that highily stringent conditions would limits the variants as claimed to structurally similar nucleic acid sequcnes. The appicant cited Huan et al 1998 and Levitan et al 1996 in support and aserts that such an approach could be use to obtain interchangable varaints of proteins (i.e. Nkx2.5/CEH-22 and SEL-12/PS1/PS2). The applicant argues that such and evidence demonstrates that applicnats specificaiton satisfies the writtern description requirements.

However, applicant's argument are found not persuasive because scope of invention as claimed is not limited to nucleic acid encoding polypeptide of SEQ ID NO:57 or SEQ ID NO:102, but a nucleic acid sequences derived from any organism that encodes a polypeptide having any insulin signaling activity. As stated earlier the disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only discloses the amino acid sequences of SEQ ID NO:57 and 102. The specification fails to disclose any variant of SEQ ID NO:54, FKHR and AFX and has the functional property of an insulin signaling polypeptide explicitly or implicitly as putatively claimed herein.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021*

(Fed. Cir. 1991). In the instant case variants of SEQ ID nO:57 and 102 as claimed has been defined only by a statement of function that broadly encompasses an insulin signaling like activity, which conveyed no distinguishing information about the identity of the claimed genetic sequence, such as its relevant structural or physical characteristics like regulatory regions and the genomic sequence etc. The scope of invention as claim also encompasses any variation in the conserved motif (SEQ ID NO:55 or 102), which is considered germane to the functional activity of the encoded polypeptide. For example any variation in the conserved domain of a hybridization product as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo and Rudinger). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member (daf-16 motif) of this genus is not representative of the variants of genus (all related genes) and is insufficient to support the claim.

Claims 17 and 19-20 and 23-24 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the same reasons of record as set forth in the office action mailed on 07/22/05.

Nature of Invention:

The instant invention relates to a method for identifying a compound that ameliorate or delay an impaired glucose tolerance condition atherosclerosis or obesity.

Breadth of Claims and Guidance Provided in the Specification

The instant claims are drawn to a method for screening candidate modulatory compounds for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity comprising: providing a C. elegans or isolated C. elegans cell expressing a gene that encodes any variant of SEO ID NO:54, SEQ ID NO:57, SEQ ID NO:102, human FKHR polypeptide or human AFX polypepide that functions in insulin signaling; and contacting the C. elegans or isolated C. elegans cell with a candidate compound, wherein a decrease in expression or activity of the gene with the candidate compound identifies a candidate modulatory compound for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity.

At best the specification discloses the amino acid sequences of SEQ ID NO:54 which represent an amino acid motif at location 242-344 of *C. elegans* daf-16 protein (spec. page 77, para.2). Based upon the degree of amino acid homology (Spec. fig-21A), the specification teaches that FKHR and AFX are human orthologs of *C. elegans's* daf-16 (Spec. fig-21B). Besides the amino acid sequences of SEQ ID NO:54 **(def-16 motif)** the specification as filed fails to disclose what encompass a nucleic acid comprising any variant of SEQ ID NO:54 that functions in any insulin signaling pathway. Similarly the specification as filed fails to disclose any nucleic acid comprising any variant of SEQ ID NO:57 and 102 that hybridizes under stringent conditions to the nucleic acid encoding the amino acid sequences of SEQ ID NO:57 and 102 respectively and is capable of performing the asserted biological activity. *Furthermore, besides human FKHR and AFX encoding sequences the specification fails to disclose any other nucleic acid sequence that is a variant of SEQ ID NO:57 and SEQ:102, wherein the gene is obtained form any other organism and is capable of functioning like an insulin signals and convergence with DAF-7-like Smad signals. The specification as filed fails to identify the relevant characteristics of the nucleic acid sequences (as claimed) such that a person skilled in the art would recognize the other human FKHR and human AFX related nucleic acid sequences.*

Response to arguments

Regardng claims 1, 21 and 22 the applicant arguments has been found persuasive as claims has been amended to recite a human AFX or human FKHR polypeptides (rather than human AFX or human FKHR genes(s)). Regarding claim 1 (95% identity) the applicants arguments has been found persusive in view of fact that daf-16 is 71% identical to daf-16 and Dr. Gary Ruvkuns decllaration that demonstrated that FKHR can fucntionally substitute dor daf-16 in vivo.

Regarding 17 (hybridization variant) the applicant argues that the experimentation required to identfy other nucleic acid sequnces encoding the polypeptided recited in claim 17 is routine in molecular biology and therefore does not constitute undue experimentation. The applicant argues that in view of Dr. Ruvkun's decleartion and in view of Huan et al 1998 and Levitan et al 1996, one would be able to obtain varaints as claimed that can function to provide insulin-signaling activity that is similar to C.elegans daf-16 polypeptides. However this is found not persusive because the stingent conditions as claimed in the instant case are relative thus would lead to an undue amount of experementation to practice the invention as claimed.

For example a hybridization product that encompasses any variation in the conserved domain AFX or FKHR polypeptides would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo and Rudinger). According to these facts, one skill in the art would conclude that it would require an undue amount of experimentation to practice the instant invention, since the description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim. Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore

skepticism raised in the enablement rejections are those raised in the art by artisans of expertise. In instant case identification of candidate compounds that ameliorate or delay an impaired glucose tolerance condition, atherosclerosis or obesity by evaluating the expression of a polypeptide encoded by an uncharacterized daf-16, AFX or FKHR like polypeptide is not considered routine in the art and without sufficient guidance to the nucleic acid sequence i.e. conserved domain required for the asserted insulin signaling activity the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Conclusion

Claims 17, 19-20 and 23-24 are rejected.

Claim 1, 13, 21-22 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**

SUMESH KAUSHAL
PRIMARY EXAMINER
ART UNIT 1633